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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known	
		Application Number	10/789,222
		Filing Date	February 27, 2004
		First Named Inventor	Qin Yu
		Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
Sheet 1 of 9	Attorney Docket Number	UPN0003-100 (P3115)	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	AA	FOLKMAN, "Tumor angiogenesis: therapeutic implications," New. Eng. J. Med. (1971) 285:1182-1186	
	AB	RISAU, "Mechanisms of angiogenesis," Nature (1997) 386:671-674.	
	AC	KIM, et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumor growth in vivo," Nature (1993) 362:841-844.	
	AD	HANAHAN and FOLKMAN, "Patterns and emerging mechanisms for the angiogenic switch during tumorigenesis," Cell (1996) 86:353-364.	
	AE	HANAHAN, "Signalling vascular morphogenesis and maintenance," Science (1997) 277:48-50.	
	AF	HANAHAN and WEINBERG, "The hallmarks of cancer," Cell (2000) 100:57-70.	
	AG	FOLKMAN and D'AMORE, "Blood vessel formation: what is its molecular basis?", Cell (1996) 87:1153-1155.	
	AH	YANCOPOULOS, et al., "Vascular-specific growth factors and blood vessel formation," Nature (2000) 407:242-248.	
	AI	INGBER and FOLKMAN, "How does extracellular matrix control capillary morphogenesis?", Cell (1989) 58:803-805.	
	AJ	RAMSAUER and D'AMORE, "Getting tie(2)d up in angiogenesis," J. Clin. Investig. (2002) 110:1615-1617.	
	AK	BETSHOLTZ, et al., "Developmental roles of platelet -derived growth factors," BioEssays (2001) 23:494-507.	

Examiner Signature		Date Considered	6/11/06
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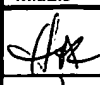

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	AL	FONG, et al., "Role of the Flt-1 receptor tyrosine kinase in regulating the assembly of vascular endothelium," Nature (1995) 376:66-70.	
	AM	MAISONPIERRE, et al., "Angiopoietin-2, a natural antagonist for tie2 that disrupts in vivo angiogenesis," Science (1997) 277:55-60.	
	AN	SATO, et al., "tie-1 and tie-2 define another class of putative receptor tyrosine kinase genes expressed in early embryonic vascular system," Proc. Natl. Acad. Sci. USA (1993) 90:9355-9358.	
	AO	SCHNURCH and RISAU, "Expression of the tie-2, a member of a novel family of receptor tyrosine kinases, in the endothelial cell lineage," Development (1993) 119:957-968.	
	AP	DUMONT, et al., "Dominant-negative and targeted null mutations in the endothelial receptor tyrosine kinase, tek, reveal a critical role in vasculogenesis of the embryo," Genes Dev. (1994) 8:1897-1909.	
	AQ	COOGAN, et al., "Expression of tie2/tek in breast tumor vasculature provides a new marker for evaluation of tumor angiogenesis," Br. J. Cancer (1998) 77:51-58.	
	AR	SATO, et al., "Distinct roles of the receptor tyrosine kinases tie-1 and tie-2 in blood vessel formation," Nature (1995) 376:70-74.	
	AS	SURI, et al., "Requisite role of angiopoietin-1, a ligand for the TIE2 receptor during embryonic angiogenesis," Cell (1998) 87:1171-1180.	
	AT	GALE and YANCOPOULOS, "Growth factors acting via endothelial cell-specific receptor tyrosine kinases: VEGFs, angiopoietins, and ephrins in vascular development," Genes Dev. (1999) 13:1055-1066.	
	AU	SURI, et al., "Increased vascularization in mice overexpressing angiopoietin-1," Science (1998) 282:468-471.	
	AV	THURSTON, et al., "Leakage-resistant blood vessels in mice transgenically overexpressing angiopoietin-1," Science (1999) 286:2511-2514.	

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<i>AK</i>	AW	THURSTON, et al., "Angiopoietin-1 protects the adult vasculature against plasma leakage," Nature Med. (2000) 6:460-463.	
	AX	STRATMANN, et al., "Cell type-specific expression of angiopoietin-1 and angiopoietin-2 suggests a role in glioblastoma angiogenesis," Am. J. Pathol. (1998) 153:1459-1466.	
	AY	WITZENBICHLER, et al., "Chemotactic properties of angiopoietin-1 and -2, ligands for the endothelial-specific receptor tyrosine kinase tie2," J. Biol. Chem. (1998) 273:18514-18521.	
	AZ	CARLSON, et al., "Direct cell adhesion to the angiopoietins mediated by integrins," J. Biol. Chem. (2001) 276:26518-26525.	
	BA	PAPAPETROPOULOS, et al., "Angiopoietin-1 inhibits endothelial cell apoptosis via the Akt/survivin pathway," J. Biol. Chem. (2000) 275:9102-9105.	
	BB	KIM, et al., "Angiopoietin-1 regulates endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway," Circulation Res. (2000) 86:24-29.	
	BC	HAYES, et al., "Angiopoietin-1 and its receptor Tie-2 participate in the regulation of capillary-like tubulin formation and survival of endothelial cells," Microvasc. Res. (1999) 58:224-237.	
	BD	OH, et al., "Hypoxia and vascular endothelial growth factor selectively upregulate angiopoietin-2 in bovine microvascular endothelial cells," J. Biol. Chem. (1999) 274:15732-15739.	
	BE	MANDRIOTA and PEPPER, "Regulation of angiopoietin-2 mRNA levels in bovine microvascular endothelial cells by cytokines and hypoxia," Circulation Res. (1998) 83:852-859.	
	BF	KIM, et al., "Tumor necrosis factor-alpha upregulates angiopoietin-2 in human umbilical vein endothelial cells," Biochem. Biophys. Res. Comm. (2000) 269:361-365.	
<i>c</i>	BG	KIM, et al., "Angiopoietin-1 induces endothelial cell sprouting through the activation of focal adhesion kinase and plasmin secretion," Circulation Res. (2000) 86:952-959.	

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	BH	VALENZUELA, et al., "Angiopoietins 3 and 4: diverging gene counterparts in mice and humans," Proc. Natl. Acad. Sci. USA (1999) 96:1904-1909.	
	BI	SIEMEISTER, et al., "Two independent mechanisms essential for tumor angiogenesis: inhibition to human melanoma xenograft growth by interfering with either the vascular endothelial growth factor receptor pathway of the tie-2 pathway," Cancer Res. (1999) 59:3185-3193.	
	BJ	MILLAUER, et al., "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant," Nature (1994) 367:576-579.	
	BK	GOLDMAN, et al., "Paracrine expression of a native soluble vascular endothelial growth factor receptor inhibits tumor growth, metastasis, and mortality rate," Proc. Natl. Acad. Sci. USA (1998) 95:8795-8800.	
	BL	AHMAD, et al., "The effects of angiopoietin-1 and -2 on tumor growth and angiogenesis in human colon cancer," Cancer Res. (2001) 61:1255-1259.	
	BM	ETOH, et al., "Angiopoietin-2 is related to tumor angiogenesis in gastric carcinoma: possible in vivo regulation via induction of proteases," Cancer Res. (2001) 61:2145-2153.	
	BN	HAWIGHORST, et al., "Activation of the tie2 receptor by angiopoietin-1 enhances tumor vessel maturation and impairs squamous cell carcinoma growth," Am. J. Pathol. (2002) 100:1381-1392.	
	BO	KOGA, et al., "Expression of angiopoietin-2 in human glioma cells and its role for angiogenesis," Cancer Res. (2001) 61:6248-6254.	
	BP	PAPETTI and HERMAN, "Mechanisms of normal and tumor-derived angiogenesis," Am. J. Physiol. Cell Physiol. (2002) 282:C947-C970.	
	BQ	TEICHERT-KULISZEWSKA, et al., "Biological action of angiopoietin-2 in a fibrin matrix model of angiogenesis is associated with activation of Tie2," Cardiovasc. Res. (2001) 49:659-670.	

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VIA	BS	YU and STAMENKOVIC, "Localization of matrix metalloproteinase 9 to the cell surface provides a mechanism for CD44-mediated tumor invasion," Genes Dev. (1999) 13:35-48.	
	BT	HUNGERFORD and LITTLE, "Developmental biology of the vascular smooth muscle cell: building a multilayered vessel wall," J. Vasc. Res. (1999) 36:2-27.	
	BU	GALE, et al., "Angiopoietin-2 is required for postnatal angiogenesis and lymphatic patterning, and only the latter role is rescued by angiopoietin-1," Devel. Cell (2002) 3:411-423.	
	BV	SHYU, et al., "Direct Intramuscular injection of plasmid DNA encoding angiopoietin-1 but not angiopoietin-2 augments revascularization in the rabbit ischemic hindlimb," Circulation (1998) 98:2081-2087.	
	BW	KIM, et al., "Angiopoietin-2 at high concentration can enhance endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway," Oncogene (2000) 19:4549-4552.	
	BX	LANDER and SELLECK, "The elusive functions of proteoglycans: in vivo veritas," J. Cell Biol. (2000) 148:227-232.	
	BY	IOZZO, "Matrix metalloproteins: from molecular design to cellular function," Ann. Rev. Biochem. (1998) 67:609-652.	
	BZ	IOZZO and SAN ANTONIO, "Heparan sulfate proteoglycans: heavy hitters in the angiogenesis arena," J. Clin. Invest. (2001) 108:349-355.	
	CA	FIEDLER, et al., "Angiopoietin-1 and angiopoietin-2 share the same binding domains in the tie-2 receptor involving the first Ig-like loop and the epidermal growth factor-like repeats," J. Biol. Chem. (2003) 278:1721-1727.	
	CB	YU, et al., "Induction of apoptosis of metastatic mammary carcinoma cells in vivo by disruption of tumor cell surface CD44 function," J. Exp. Med. (1997) 188:1985-1998.	
	CC	KONTOS, et al., "Tyrosine 1011 of tie2 is the major site of association of p85 and is required for activation of phosphatidylinositol 3-kinase and Akt," Mol. Cell. Biol. (1998) 18:4131-4140.	

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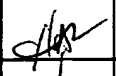

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	CD	FIDLER and ELLIS, "The Implications of angiogenesis for the biology and therapy of cancer metastasis," Cell (1994) 78:185-188.	
	CE	FIDLER, "Angiogenetic heterogeneity: regulation of neoplastic angiogenesis by the organ microenvironment," J. Natl. Cancer Inst. (2001) 93:1040-1041.	
	CF	ALI, et al., "Estrogen receptor-alpha in the inhibition of cancer growth and angiogenesis," Cancer Res. (2000) 60:7094-7098.	
	CG	NOKIHARA, et al., "Natural killer cell-dependent suppression of systemic spread of human lung adenocarcinoma cells by monocyte chemoattractant protein-1 gene transfection in severe combined immunodeficient mice," Cancer Res. (2000) 60:7002-7007.	
	CH	LINDAHL, et al., "Pericyte loss and microaneurysm formation in PDGF-B-deficient mice," Science (1997) 277:242-245.	
	CI	GENGRINOVITCH, et al., "Glypican-1 is a VEGF165 binding proteoglycan that acts as an extracellular chaperone for VEGF165," J. Biol. Chem. (1999) 274:10816-10822.	
	CJ	LI, et al., "Increased responsiveness of hypoxic endothelial cells to FGF2 is mediated by HIF-1alpha-dependent regulation of enzymes involved in synthesis of heparan sulfate FGF2-binding sites," J. Cell Sci. (2002) 115:1951-1959.	
	CK	NEUFELD, et al., "Vascular endothelial growth factor (VEGF) and its receptors," FASEB J. (1999) 13:9-22.	
	CL	PARK, et al., "The vascular endothelial growth factor (VEGF) isoforms: differential deposition into the subepithelial extracellular matrix and bioactivity of extracellular matrix-bound VEGF," Mol. Biol. Cell (1993) 4:1317-1328.	
	CM	PEPPER, et al., "Transforming growth factor-beta: vasculogenesis, angiogenesis, and vessel wall integrity," Cytokine Growth Factor Rev. (1997) 8:21-43.	
	CN	XU and YU, "E-cadherin negatively regulates CD44-hyaluronan interaction and CD44-mediated tumor invasion and branching morphogenesis," J. Biol. Chem. (2003) 278:8661-8668.	

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AK	CO	POLTORAK, et al., "VEGF145, a secreted vascular endothelial growth factor isoform that binds to extracellular matrix," J. Biol. Chem. (1997) 272:7151-7158.	
	CP	ROBINSON and STRINGER, "The splice variants of vascular endothelial growth factor (VEGF) and their receptors," J. Cell Sci. (2001) 114:853-865.	
	CQ	RUHRBERG, "Endogenous inhibitors of angiogenesis," J. Cell Sci. (2001) 114:3215-3216.	
	CR	SAARISTO, et al., "Mechanisms of angiogenesis and their use in the inhibition of tumor growth and metastasis," Oncogene (2000) 19:6122-6129.	
	CS	MAESHIMA, et al., "Tumstatin, an endothelial cell-specific inhibitor of protein synthesis," Science (2002) 295:140-143.	
	CT	O'REILLY, et al., "Angiostatin: a novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma," Cell (1994) 79:315-328.	
	CU	O'REILLY, et al., "Antiangiogenic activity of the cleaved conformation of the serpin antithrombin," Science (1999) 285:1926-1928.	
	CV	YI and RUOSLAHTI, "A fibronectin fragment inhibits tumor growth, angiogenesis, and metastasis," Proc. Natl. Acad. Sci. USA (2001) 98:820-824.	
	CW	VU, et al., "MMP-9/gelatinase-B is a key regulator of growth plate angiogenesis and apoptosis of hypertrophic chondrocytes," Cell (1998) 93:411-422.	
	CX	VAJKOCZY, et al., "Microtumor growth initiates angiogenic sprouting with angiogenic sprouting with simultaneous expression of VEGF, VEGF receptor-2, and angiopoietin-2," J. Clin. Investig. (2002) 109:777-785.	
	CY	BLOEMENDAL, et al., "New strategies in anti-vascular cancer therapy," Eur. J. Clin. Investig. (1999) 29:802-809.	

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Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
<i>AK</i>	CZ	HARFOUCHE, et al., "Mechanisms which mediate the antiapoptotic effects of angiotensin-1 on endothelial cells," Microvasc. Res. (2002) 64:135-147.	
	DA	HIRAOKA, et al., "Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins," Cell (1998) 95:365-377.	
	DB	BERGERS, et al., "Matrix metalloproteinase-9 triggers the angiogenic switch during carcinogenesis," Nature Cell Biol. (2000) 2:737-744.	
	DC	FANG, et al., "Matrix metalloproteinase-2 is required for the switch to the angiogenic phenotype in a tumor model," Proc. Natl. Acad. Sci. USA (2000) 97:3884-3889.	
	DD	PFEIFER, et al., "Suppression of angiogenesis by lentiviral delivery of PEX, a noncatalytic fragment of matrix metalloproteinase 2," Proc. Natl. Acad. Sci. USA (2000) 97:12227-12232.	
	DE	STERNLICHT and WERB, "How matrix metalloproteinases regulate cell behavior," Ann. Rev. Cell Dev. Biol. (2001) 17:463-518.	
	DF	SILLETI, et al., "Disruption of matrix metalloproteinase 2 binding to Integrin alphavbeta3 by an organic molecule inhibits angiogenesis and tumor growth in vivo," Proc. Natl. Acad. Sci. USA (2001) 98:119-124.	
	DG	SIPES, et al., "Cooperation between thrombospondin-1 type 1 repeat peptides and alphavbeta3 integrin ligands to promote melanoma cell spreading and focal adhesion kinase phosphorylation," J. Biol. Chem. (1999) 274:22755-22762.	
	DH	VISCONTI, et al., "Orchestration of angiogenesis and arteriovenous contribution by angiotensins and vascular endothelial growth factor (VEGF)," Proc. Natl. Acad. Sci. USA (2002) 99:8219-8224.	
	DI	UEMURA, et al., "Recombinant angiotensin-1 restores higher-order architecture of growing blood vessels in mice in the absence of mural cells," J. Clin. Invest. (2002) 110:1619-1628.	
<i>✓</i>	DJ	YU and STMENKOVIC, "Cell surface-localized matrix metalloproteinase-9 proteolytically activates TGF-beta and promotes tumor invasion and angiogenesis," Genes Dev. (2000) 14:163-176.	

Examiner Signature	<i>[Signature]</i>	Date Considered	6/11/06
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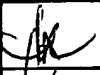
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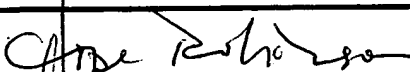
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Substitute for form 1449B/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	10/789,222
		Filing Date	February 27, 2004
		First Named Inventor	Qin Yu
		Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
		Attorney Docket Number	UPN0003-100 (P3115)
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Sheet	9	of	9

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	DK	McFALL and RAPRAEGER, "Characterization of the high affinity cell-binding domain in the cell surface proteoglycan syndecan-4," J. Biol. Chem. (1998) 273:28270-28276.	
	DL	OLSON, et al., "High affinity binding of latent matrix metalloproteinase-9 to the alpha2(IV) chain of collagen IV," J. Biol. Chem. (1998) 273:10672-10681.	
	DM	BROOKS, et al., "Localization of matrix metalloproteinase MMP-2 to the surface of invasive cells by interaction with integrin alphavbeta3," Cell (1996) 85:683-693.	
	DN	MOYON, et al., "Selective expression of angiopoietin 1 and 2 in mesenchymal cells surrounding veins and arteries of the avian embryo," Mech. Dev. (2001) 106:133-136.	
	DO	WONG, et al., "Tie2 expression and phosphorylation in angiogenic and quiescent adult tissues," Circ. Res. (1997) 81:567-574.	
	DP	SHIM, et al., "Inhibition of angiopoietin-1 expression in tumor cells by an antisense RNA approach inhibited xenograft tumor growth in immunodeficient mice," Int. J. Cancer (2001) 94:6-15.	
	DQ	SHIM, et al., "Angiopoietin 1 promotes tumor angiogenesis and tumor vessel plasticity of human cervical cancer in mice," Exp. Cell Res. (2002) 279:299-308.	
	DR	JOUSSEN, et al., "Suppression of diabetic retinopathy with angiopoietin-1," Am. J. Pathol. (2002) 160:1683-1693.	
	DS	HATTORI, et al., "Vascular endothelial growth factor and angiopoietin-1 stimulate postnatal hematopoiesis by recruitment of vasculogenic and hematopoietic stem cells," J. Exp. Med. (2001) 193:1005-1014.	
	DT	DAVIS, et al., "Angiopoietins have distinct modular domains essential for receptor binding, dimerization and superclustering," Nature Struct. Biol. (2002) 10:38-44.	

Examiner Signature		Date Considered	6/11/06
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Filing Date	February 27, 2004
First Named Inventor	Qin Yu
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	DU	KOVESDI et al., Database GenCore, Accession No. AAE32344, 10-24-2002, Gene Sequence.	
	DV	International Search Report Dated January 14, 2005 for International Application No. PCT/US04/06101.	

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